REMARKS

Claims 4, 6, and 7 presently appear in this case. No claims have been allowed. The Official Action of November 21, 2008, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method for detecting the presence of a target single-stranded nucleic acid in a sample. The sample suspected of containing the target single-stranded nucleic acid is first brought into contact with a nucleic acid probe that is a DNA fragment or a chemically synthesized DNA that includes a nucleic acid sequence complimentary to the target single-stranded nucleic acid, under hybrization conditions. The result is a double stranded hybrid nucleic acid that appears only when the target nucleic acid is present in the sample. A cationic dye compound of specified formula is then added which will bind to any double stranded DNA present in the reaction mixture. Circular dichroism will only manifest itself if the target single-stranded nucleic acid was present in the sample. Therefore, one can determine that the target was present in the sample simply by measuring the circular dichroism.

Claims 4, 6 and 7 have been rejected under 35 USC 103a as being unpatentable over Larsson in view of Juarrenz. The examiner states that Larsson detects hybrid nucleic acid, which by definition is double stranded, by use of a cationic dye compound. The examiner interprets Larsson's double stranded DNA as including one strand which is the target and another strand which is the probe. The examiner considers that this double stranded DNA is inherently obtained as a result of carrying out a method step of bringing a nucleic acid probe in a sample containing a target nucleic acid into contact with each other under hybrization conditions. The

examiner acknowledges that Larsson does not teach the cationic dye compound presently claimed but the examiner considers that it would be obvious to substitute the dye compound of Juarrenz for that of Larsson. This rejection is respectfully traversed.

Claim 4 has now been amended to clarify that the present invention is a method for detecting the presence of a target single-stranded nucleic acid in a sample. The new claim language is supported by the last paragraph on page 17 of the specification, which refers to a method of detection and clarifies that if no hybrid is formed, namely, if DNA remains to be a single-strand, the circular dichroism peak will not appear. This language clearly distinguishes the method of the present invention from that of Larsson, which is not an assay and does not and cannot detect single-stranded nucleic acid. No single-stranded nucleic acid is present in any part of the disclosure of Larsson or Juarrenz.

Claim 4 has further been amended to specify that there is a contacting step that requires contacting a sample suspected of containing a target single-stranded nucleic acid with a nucleic acid probe that is complimentary thereto under hybridization conditions. Again, Larsson does not do this. The examiner states that Larsson's hybrid DNA must have been made by such a step, but this is not so. Larsson states in the paragraph bridging pages 8459 and 8460 that the double stranded DNA as is used in their study were merely purchased from Sigma or from New England Bio Lab. There is no evidence that Sigma or New England Bio Lab made this double stranded DNA by synthesizing a forward strand and a complimentary strand and then hybridizing them. More likely, they are fragments of a naturally occurring double stranded DNA. Certainly, the examiner has now established a prima facie case that Sigma or New England Bio Lab necessarily made their double-stranded product by hybridization of two

complementary single strands.[1] In order for there to be a rejection based on inherency, the inherency must be certain, not merely based on possibilities or probabilities. See MPEP 2112 IV. Larsson does not include a step of bring a nucleic acid probe into contact with a target nucleic acid. For this reason alone, no combination of Larsson with Juarrenz teaches or makes obvious the process of the present invention, particularly as presently claimed.

Besides the critical differences discussed above, the examiner impermissibly ignores the art-recognized meaning of the term "nucleic acid probe." The examiner interprets the term so broadly as to include any strand of a double stranded DNA. Such a strained interpretation is not permitted by the law. MPEP paragraph 2111 states:

> During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification."

The key word in this sentence is "reasonable." The examiner's interpretation of the term "nucleic acid probe" is totally unreasonable and is inconsistent with the specification and the well known meaning of this term to those of ordinary skill in the art.

> The present specification states at page 19, lines 20-26:
>
> As the nucleic acid probe, there can be employed DNA fragments formed by cleaving DNA extracted from a biological sample with the use of a restriction enzyme, and purifying the cleaved pieces, for example, by electrophoretic or other separation, or chemically synthesized DNA. Preferably, the nucleic acid probe is sequenced beforehand according to a well known sequencing method.

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[1] Even if they did, this would not involve the use of a "nucleic acid probe," as is required by the claims. The definition of this term will be discussed in detail below.

This discussion and the use of the term "nucleic acid probe" throughout the specification is consistent with the art recognized definition. Submitted herewith is the definition of "DNA Probe" at pages 101-102 of "GLOSSARY OF BIOTECHNOLOGY AND NANOBIOTECHNOLOGY TERMS," Fourth Edition, Ed. K. Nill, Taylor & Francis Group, Boca Raton, Florida 2006. It can seen that this definition begins:

> **DNA Probe** Also called gene probe or genetic probe. Short, specific (complimentary to desired gene) artificially produced segments of DNA used to combine with and detect the presence of specific genes (or shorter DNA segments) within a chromosome.

At page 303 of the same dictionary, the term "probe" is defined as follows:

> **Probe** A relatively small molecule that can be used to sense the presence and condition of a specific protein, DNA fragment, RNA fragment or nucleic acid by a unique interaction with that macromolecule.

See also the definition of "probe" at page 280 of "DICTIONARY OF BIOTECHNOLGY," Second Edition, Ed. J. Coombs, Stockton Press, New York, NY, 1992, where the first definition of "probe" begins:

> **probe** (1) in nucleic acid dependent analysis, a length of RNA or DNA used in molecular hybridization to detect complimentary sequences, by base pairing, in the presence of a large amount of non-complimentary DNA.

The term "probe" is defined at page 856 of "The Dictionary of Gene Technology: Genomics, Transcriptomics, Proteomics," Third Edition, Ed. G. Kahl, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2004, where the first definition begins (with cross reference markings omitted):

> **Probe:**
> a) a defined and radioactively or non-radioactively labeled nucleic acid sequence used in molecular cloning to identify

> specific DNA molecules with complimentary sequence(s) by autoradiography or with non-radioactive DNA-detection systems.

The examiner's interpretation bears no resemblance to these art-recognized definitions, all of which are consistent with one another. Larsson does not use a probe, nor does Larsson suggest the use of a probe. The same is true of Juarrenz. Thus, even if Sigma synthesized the two strands of coliphage T2 DNA and caused them to hybridize with one another in order to make the product that it sold to Larsson, this would still not read on the process of the present invention because neither of the synthetic strands of Sigma meet the definition of probe as discussed above. Of course, this issue is moot as Sigma does not disclose how it made the product that it sold to Larsson and the burden is on the examiner to establish a *prima facie* case of obviousness.

While the combination of references does not make obvious the presently claimed methods for all of the reasons discussed above, it should further be noted that the product of Juarrenz is not is not disclosed as being an equivalent to the YOYO of Larsson as Juarrenz does not describe CD measurement at all. Therefore, a skilled reader would not have been motivated to substitute the YOYO of Larrson, which is used for CD measurement in the process of Larrson, with the TMAP of Juarrenz, which does not describe CD detection using a cationic dye.

For all of these reasons, the present invention, particularly as presently claimed, is not made obvious by any combination of Larsson with Juarrenz. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 USC 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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